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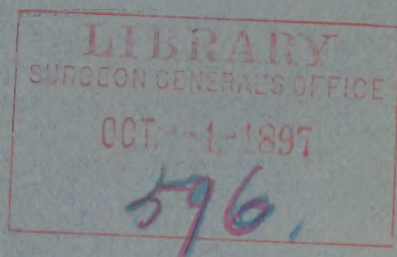
With a Consideration of its Pathology and Clinical History.

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THE observation, in two small medical services in four months, of four cases of a disease which has been hitherto unrecognized in Cleveland has seemed to us worth calling attention to. It is not improbable that, now that attention is directed to the subject, the disease will be found to be of not uncommon occurrence.

Of our four cases two gave histories of previous chronic diarrhœa, the remaining two had diarrhœa on admission, one acute and the other chronic. In the cases with diarrhœa we did not have an opportunity of examining the stools. Three cases had chronic liver-abscesses, which in two communicated with the right pleural cavity through the diaphragm. In the case with diarrhœa of recent date (Case I.) the abscess was evidently acute. In two cases the clinical diagnosis was established by autopsy, in one case by both aspiration and operation, and in one (Case I.) by aspiration. The *amœba coli* was found in two cases: in one in the evacuated pus (Case II.), and in one at the autopsy (Case IV.). In Case I., by a mistake, the pus was lost before a microscopical examination could be made. In Case IV. *amœbæ* were found in the liver-abscess in the right pleural cavity and in the pericardial cavity. In this case there was a triple bacterial mixed infection. In Case I. there was evidently a severe bacterial mixed infection, probably streptococcus. It is much to be regretted that an autopsy could not be obtained in this case. There can be no doubt that all these cases are to be regarded as cases of *amœbic* liver-abscesses secondary to dysentery. In this opinion we are supported by the occurrence of previous chronic diarrhœa in two cases, existing diarrhœa in two cases, the finding of the scars of healed ulcers in the colon of two cases coming to autopsy, and the demonstration of the *amœba coli* in two cases. All of the patients lived in Cleveland.

CASE I.—Man, aged thirty-six years, laborer, entered the Lakeside Hospital (service of Dr. Powell) May 26th, giving a history of having

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been severely ill only five days before admission to the hospital. He complained of chills, fever, and profuse sweating and pain in the right hypochondrium near the border of the ribs. Diarrhœa at present not severe; two soft movements daily, containing a large amount of mucus. Has had former attacks of severe diarrhœa; no blood in the stools. The patient suffered from daily chills and profuse sweating, with rapid rises and remissions of temperature.

On June 2d, at 3 A.M., the temperature was 106° in the axilla; at 8 A.M., 93° in the axilla. The frequent chills and rises in temperature, coming at irregular intervals of from twenty-four to forty-eight hours, persisted up to the time of death, which occurred on June 20th.

An autopsy was forbidden. Exploratory puncture in the right hypochondrium, between the ninth and tenth ribs in the anterior axillary line, yielded a pint of grayish-red pus resembling anchovy sauce. Unfortunately, through a mistake, the pus was lost, so that a microscopic examination of it was not made.

For the clinical history of the following case we are indebted to Dr. W. Rogers, with whom the patient was seen in consultation:

CASE II.—O. E., laborer, aged thirty-two years, admitted to the City Hospital May 11, 1895. The patient has been a resident of Cleveland for five years. One and one-half years ago he had a severe diarrhœa with colic and bloody stools. The diarrhœa persisted for two months. During last summer (1894) he had "pneumonia." For the past eight months he has been in a moderately good condition, until a month before admission to the hospital, when he was taken sick with diarrhœa, bloating of the abdomen, and nausea. About the same time a stitching pain in the lower right thorax in the axillary line appeared. At present the diarrhœa is not severe. The patient is very weak, has no appetite, has frequent chilly sensations, sweats profusely at nighttime, expectorates large amounts of mucopurulent sputum, marked dyspnœa. Urine acid; specific gravity 1020; no sugar or albumin.

May 14. Urine acid; specific gravity 1010; no sugar or albumin; amount, 61 oz. in twenty-four hours; urea, 216.5 grains in twenty-four hours. From the physical examination is given the following abstract: patient is emaciated; skin light and clear; face dark; conjunctivæ and mucous membrane of mouth slightly icteroid; tongue red at tip and edges, furred in the centre; pulse, small volume, rapid, low tension; thorax moderately broad and deep; abdomen prominent, especially in the epigastrium; the anterior thorax showed nothing pathological in either the heart or lungs. In the supra- and inter-scapular areas there is no essential difference between the two sides. Over the seventh and eighth ribs in the scapular line on the right side the percussion-note is dull, tympanitic in character. From the eighth rib downward the percussion-note shows an absence of resonance. Over the dull, tympanitic area in the right infrascapular region the inspiration and expiration are bronchovesicular in character. From the eighth rib downward no respiratory sounds are audible.

The liver is uniformly enlarged, reaching three fingers' breadth below the border of the ribs. At the costal border in the anterior axillary line of the right side a friction is palpable and audible, accompanying the respiratory excursion of the liver. The spleen is not palpable, but the percussion-area is enlarged. The liver is sensitive to pressure, but

the abdomen is nowhere else sensitive to pressure. During the following week the lower border of the liver ascended nearly two fingers' breadth. The patient was rapidly losing in strength.

On May 20th an exploratory puncture in the ninth intercostal space in the posterior axillary line yielded a thin yellow pus which on microscopic examination showed a relatively small number of well-preserved leucocytes. Large cells answering to the description of *amœba coli* were seen in considerable number, though no amœbic movement was seen.

On May 23d Dr. Hobson drained the abscess from the ninth interspace in the posterior axillary line—fully two pints of pus were evacuated; drainage established.

A few days later all the signs of an empyema appeared. The sweats and fever continued. The patient's strength gradually diminished. Death occurred June 11, 1895. Unfortunately, a complete record of the temperature-curve during the entire illness was not preserved. The temperature reached its highest point gradually about midnight, accompanied by profuse sweating. The highest temperature was 104.4°, a remission of five degrees occurring within six hours. From May 20–23d (day of operation) the temperature gradually descended to 98°. For eight days after the operation the temperature ranged from 97.5° to 99°. The last six days of life a subnormal temperature was constant.

Autopsy by Dr. Hoover. Anatomical diagnosis: a large abscess the size of a cocoanut in the upper portion of the right of the liver, with adhesion of the adjacent portion of the liver to the diaphragm and to the abdominal wall. A sinus admitting the point of the little finger connected the abscess-cavity with the right thorax. Acute empyema (2 quarts of thin, gray pus), compression of the right lung, chronic tuberculosis of the apex of the left lung. Limited chronic fibrous peritonitis over the descending colon and sigmoid flexure, with cicatrices; remains of old ulcers on the corresponding internal surface of the intestine. Chronic passive congestion of kidneys and spleen.

The liver-abscess was filled with a thin, grayish-yellow pus. The walls of the abscess were irregular and ragged and covered with a friable grayish necrotic material. Outside of this there was a thin zone of relatively firm fibrous tissue. The pus in the liver-abscess and in the thorax presented the same appearances.

CASE III.—J. J., male, laborer, aged thirty-two years; admitted to the City Hospital August 31 1895. Parents living and in good health. Three brothers and one sister dead; causes unknown.

The patient says he has never been sick before excepting from excessive drinking. Patient has never been south of northern Ohio. Former occupation was that of seaman on the Great Lakes. His present illness began a week before admission with a tired feeling; headache; epistaxis (not severe); occasional vomiting; insomnia (says he was delirious at times); night-sweats; no pain in the thorax; slight cough; expectorates a small amount of yellowish sputum; has been losing flesh rapidly; pain in the lower abdomen severe. The patient has frequent stools (seven a day), consisting largely of freshly clotted blood. Microscopic examination for amœbæ was negative; urine acid, specific gravity 1014; sugar, albumin, and diazo negative. The patient was seen first by the visiting physician on September 3d, ten days after the beginning of the illness (according to the patient's own account). The following observations were made at that time: the examination of the thorax re-

vealed nothing pathological. The liver encroached upon the right thorax two fingers' breadth in the axillary and scapular lines, and although the hepatic dulness extended three fingers' breadth below the costal border in the nipple-line, the edge of the liver was not palpable. Pressure under the costal border in the right hypochondrium causes pain. In the midaxillary line over the hepatic area a friction-sound is heard during the respiratory excursion of the liver. The sound is not audible in the nipple-line nor at the costal border, and is not palpable. The spleen is palpable on deep inspiration at the border of the ribs. On the following day (4th) the patient was in a state of collapse, so that an exploratory puncture of the liver was impossible. Death occurred during the morning of the 5th.

An autopsy was forbidden, but the following exploratory punctures were made. The ninth intercostal space in the midaxillary line (right side) yielded a small amount of reddish serum which contained a small amount of cell detritus and a few red blood-corpuscles. In the ninth interspace in the scapular line a moderately thick bloody pus (anchovy-sauce); microscopically a moderate amount of fat-globules; very few well preserved cells—*i. e.*, pus-cells—could be found. The only cells in a state of preservation were a few fatty degenerated liver-cells.

A third puncture in the eleventh intercostal space, posterior axillary line, gave the same result as above. Exploratory punctures were made in the seventh interspace in the nipple-line, at the eighth costal cartilage on the right side, and over the splenic area, with negative results. The search for amœbæ in the pus was negative.

The temperature was as follows: August 31st, P.M., 100.5°. September 1st, A.M., 99.2°; P.M., 101.2°. 2d, A.M., 98.5°; P.M., 100.2°. 3d, A.M., 97.6°; P.M., 100.8°. 4th, A.M., 97.2°; P.M., 100°. 5th, A.M., 97.4°.

CASE IV.—O. W. H., male, aged fifty-four years; occupation carpenter; admitted to City Hospital July 18, 1895. The patient lived in Cleveland twenty years preceding his death, never having been more than a few miles from the city during the entire time. There is no history of tuberculosis in his family. He denies ever having had syphilis. Had typhoid fever twenty years ago. Has had occasional "rheumatism of his joints," though there are no traces of arthritis at present visible. Drank large amounts of whiskey until two years ago, since which time he has drunk very little. During the preceding fall (1894) he had an attack of severe diarrhœa accompanied by colic. This lasted about a month; with the cessation of the diarrhœa he noticed that he voided an unusually large amount of urine each day. In a month after the diarrhœa ceased he had largely regained his former strength, and with the exception of occasional attacks of pain in the hepatic region (which were accompanied by dyspnœa) lasting several days at a time, he was in relatively fair condition until two weeks before admission to the hospital, when severe pain in the right hypochondrium and inferior right thoracic region set in. The pain has been persistent; shortness of breath has also been annoying. While going about he has noticed that the dyspnœa increased toward evening, when he noticed occasional slight swelling about the ankles. Patient has slight cough, with slight mucous expectoration. There are two to four loose movements of the bowels a day.

Urine: specific gravity 1020; acid; no albumin or sugar. Physical

examination made on July 25, 1895: development good; nourishment poor; small amount of panniculus adiposus; skin harsh and dry; yellowish pigmentation of entire skin. Both inguinal glands and the left axillary glands are about the size of a small hazelnut. No icterus; slight cyanosis. Dilatation of peripheral vessels of both cheeks; no œdema; no tenderness or thickening of the long bones. The right lateral vein of the thorax is dilated. Immediately above the umbilicus is a slight protrusion the size of a ten-cent piece which feels much like a coil of veins (*caput Medusæ*). The respiration is largely thoracic in character and increased in frequency. Thorax is moderately broad and deep. The right side in the inferior area is slightly retarded in the respiratory excursion, the difference in the two sides being very slight.

The intercostal spaces in the right hypochondrium are flattened out; in the left side they are retracted. Heart's apex-impulse is visible in the fourth interspace in the nipple line. Pulse has a moderate rate, is rhythmic, regular, small wave; short duration; easily compressible. Atheroma of both radials is pronounced.

Percussion: upper border of the heart is at the third rib in the left parasternal line; left border of the heart in the nipple-line, the right border at the left border of the sternum. The percussion-note in the right supraclavicular space is slightly less resonant than in the left. In the infraclavicular and second interspaces on the two sides there is no essential difference. There are increase of resistance and diminution of resonance toward the base on the right side. The lower border of the lung on the right side is on the fourth rib in the nipple-line, and the fourth interspace in the axillary line; respiratory excursion is present, though diminished in degree. The lower border of the left lung in the axillary line is on the seventh rib.

Posterior thorax: on the right side there are slight increase of resistance and diminution of resonance toward the base of the lung. The lower border is on the eighth rib in the scapular line; on the left side the lower border of the lung is at the tenth rib in the scapular line. The respiratory sounds are relatively loud over the entire pulmonary area, excepting at the right base, where the intensity of the respiratory and expiratory sounds is much diminished. Nowhere are there any adventitious sounds audible.

Abdomen is protruding, everywhere tympanitic; no free fluid. The right hypochondrium is sensitive to pressure. The hepatic dulness is seven inches in the nipple-line and only two fingers' breadth below the border of the ribs. In the axillary line it measures eight inches. A distinct hepatic border is not palpable, though the movement of the liver on respiration is visible below the costal border. The abdominal wall is tense and resistant.

Splenic dulness is at the eighth rib in the axillary line and extends forward to within two fingers' breadth of the costal border. The spleen is not palpable on deep inspiration.

Hemorrhoids are present; no bleeding at present. The condition of the patient remained much the same without any notable change during the month of August. Being away on a vacation during the latter part of August and first week in September, I was surprised to find on September 6th that the dyspnœa had increased, and that from the clavicle downward on the right side the thorax was flat on percussion, with total absence of vocal fremitus and respiratory sounds. The flat percussion-

note reached as far as the left border of the sternum above the pre-cardial area. Three pints of bloody pus were aspirated from the right thorax, after which the upper half of the sternum became resonant. The upper right thorax gave slight resonance on percussion and the respiratory sounds were faintly audible.

From this time the patient failed rapidly. He protested against a second aspiration of the thorax. The fluid again increased in quantity. Death occurred on the morning of September 21st.

The temperature during the first five days gradually fell from evening exacerbations to 101° and morning remissions to 99° to a continuous normal temperature. After the empyema was discovered (ten days before death), the temperature was as follows: September 11th, P.M., 99.2° . 12th, A.M., 98.5° ; P.M., 99.8° . 13th, A.M., 96.4° ; P.M., 99.2° . 14th, A.M., 96.4° ; P.M., 99° . 15th, A.M., 96° ; P.M., 95° . 16th, A.M., 95° ; P.M., 94.8° . 17th, A.M., 95° ; P.M., 95.2° . 18th, A.M., 94.8° ; P.M., 94.8° . 19th, A.M., 94.6 ; P.M., 94.6° . 20th, A.M., 94° ; P.M., 95.6° .

The pus aspirated from the thorax was examined for amœba, but none were found. From the history of the patient for the interval during which he was not under my observation it was impossible to determine the date of the origin of the empyema.

Autopsy by Dr. Howard. Anatomical diagnosis: abscess of the right lobe of the liver, with perforation of the diaphragm and empyema of the right side. Chronic pleuritis with retraction of the right lung. Chronic obliterative pleuritis of the left side. Slight chronic morbus Brightii. General heart hypertrophy and dilatation. Acute fibrinopurulent pericarditis. Scars of old ulcers in the colon. Chronic passive congestion of the spleen, kidneys, stomach, and intestines.

Autopsy eight hours after death: body still warm, 170 cm. long, very much emaciated. Subcutaneous fat and muscles wasted. There are no bedsores. The lower portion of both tibiæ rough and irregular, and the skin here of a reddish-brown color. There is no jaundice; the skin is very pale.

The right chest and hypochondrium much larger than the left. The abdomen is not distended.

The peritoneum is everywhere smooth, moist; no excess of fluid. The right lobe of the liver extends 5 cm. below the costal margin in the mammary line. The outer border and a considerable portion of the anterior surface of this lobe are bound by firm adhesions to the adjacent abdominal wall. The left lobe is larger than normal. The upper border of the right kidney is firmly adherent to the lower surface of the right lobe.

Chest: both sides free from œdema. The muscles are markedly wasted and pale. On removing the sternum a large amount of blood-stained, thin fluid escapes from the upper portion of the right pleural cavity. The outer layer of the pericardium is firmly bound by adhesions to the adjacent borders of the lungs. The pericardial cavity contains about 100 c.cm. of blood-stained pus. Both the epi- and pericardium are covered with a layer of fibrous material of varying thickness, which is thickest over the surface of the right ventricle. It is readily removed with the finger, and the underlying membrane is congested and shows many points of ecchymosis. The heart weighs 375 grammes. The wall of the left ventricle averages 17 mm. in thickness.

The heart-muscle is pale and tears with ease. The valves and the coronary arteries are normal. The aorta is somewhat dilated.

The left lung, firmly bound down by old adhesions, is voluminous, deeply pigmented, and on section œdematous. It is free from tuberculosis. The bronchial glands are pigmented.

The right pleural sac is distended with fluid. In the upper portion of the cavity there is about half a litre of thin, blood-stained fluid. Below this the rest of the cavity is filled with a thick, brownish-red, anchovy-sauce-like pus containing small, grayish, gelatinous-like masses of tissue.

Both layers of the pleura are everywhere covered with a thick layer of fibrinous material. On the lower portion of this cavity the costal and visceral pleurae, as well as the diaphragmatic layer, are very much thickened. The lung is flattened out against the posterior portion of the chest, and is firm, dense, and airless, and on section is carnified in appearance. There is no communication between the bronchi and the pleural cavity. The bronchi, veins, and arteries are of ordinary appearance.

Through an opening in the central portion of the diaphragm, large enough to admit the hand, the right pleural cavity communicates with an abscess-cavity in the upper portion of the right lobe of the liver.

The lung, pleura, diaphragm, liver, and right kidney removed *en masse*.

On section the greater portion of the right lobe of the liver is found to be the seat of an abscess, which at its lower posterior portion nearly reaches the surface of the organ. At the lower border of this lobe the abscess again reaches the surface, and at this point the upper border of the right kidney is firmly adherent to the surface of the organ. Just above this the transverse colon is adherent to the adjacent surface of this lobe by rather easily broken-down recent adhesions. There is no apparent relation between the colon and the liver-abscess. The thickness of the hepatic tissue between the wall of the abscess and the surface of the organ varies in different places from 0.5 to 7 cm., the thinnest places being near the upper and the posterior surfaces.

The wall of the abscess is in general ragged and irregular. The superficial layer is soft, easily broken down under the finger, grayish-white in appearance, and varies from 0.5 to 2 cm. in thickness. Beneath is a firmer zone of a peculiar gelatinous appearance and consistency. Outside of this there is a fibrous tissue zone of a varying thickness. The liver-tissue about this is pale and firm. The left lobe is larger than ordinary. The surface is smooth; the capsule is not thickened. On section the surface is pale and has a nutmeg appearance. The consistency is not increased. No other abscess was found. The liver measures 28 x 20 x 16 cm.

The spleen is considerably enlarged and weighs 350 grammes. The surface is smooth and free from adhesions. The capsule is not thickened. On section the tissue is soft and dark red in color. The trabeculae are visible; the Malpighian bodies are obscured.

The kidneys are of about the same size and general appearance, and somewhat smaller than ordinary. The capsules are lightly adherent in places. On the surface of the left there are several small cysts. The cortices are somewhat thinned. The consistency is not specially increased. The arteries are normal. The renal pelves, the suprarenal

bodies, bladder, penis, and testes are normal. The pancreas is normal, as are the pharynx and œsophagus. The mucous membrane of the stomach and small intestine is deeply congested. There are no scars or ulcers in the small intestine. In the rectum, sigmoid flexure, and the ascending colon there are numerous firm scars, but no fresh ulcers. About several of these scars the muscular coat is thinned.

Microscopical examination of the pus from the right pleural cavity, the liver-abscess, and from the pericardium shows large numbers of amœbæ, many of which are actively motile. They vary in size from 30 to 40 and even 50μ in diameter. In the finely granular protoplasm of many a nucleus can be made out; many contain red blood-corpuscles and pigment; few contain bacteria. Scrapings made from the pleura and pericardium show large numbers of polymorphous nuclear leucocytes, many of which contain fine fat-drops.

In the pus from the liver-abscess no leucocytes are seen. There are a few red blood-cells, some markedly fatty liver-cells, and a few amœbæ. Most of the material is made up of granular detritus. Scrapings of the wall of the abscess contain more amœbæ than the free pus.

Stained cover-slip preparations made from the liver-abscess and from the pus from the pleura and pericardium show small numbers of diplococci, a short, stout bacillus, and a long, thin bacillus. They are more numerous in the pus from the pleural sac than from the liver-abscess or from the pericardium.

In cultures made from the pus from the liver-abscess and from the pleural and pericardial pus there developed colonies of the colon-bacillus and the staphylococcus pyogenes aureus. The cultures made from the spleen and kidneys remained sterile.

Fresh frozen sections of the heart-muscle show a well-marked fatty degeneration.

Microscopical examination of sections made from various portions of the wall of the liver-abscess and stained in hæmatoxylin and eosin shows in all practically the same characters. The inner zone nearest the abscess-cavity is made up of a layer of varying depth composed largely of a granular structureless material that stains rather diffusely with both hæmatoxylin and eosin. In this material there are irregularly scattered areas composed of small round cells with round or oval nuclei, and a smaller number of spindle-shaped cells. The round cells predominate. The cells extend in some places deep into the underlying tissue, but in other places they are confined to the margin of the abscess-wall. In this zone, in its superficial portion, here and there a few large cells can be made out—amœbæ. Beneath this zone of necrosis there is a broad band of fibrous tissue very poor in cells. In places the necrotic zone extends into this layer. In the outer portion of the fibrous tissue layer there are a few bands or single rows of elongated liver-cells to be seen. There are here and there also many small bile-ducts made out. Outside the fibrous tissue zone the liver-cells are compressed and have lost their shape. The acini can nowhere be made out. The liver-cells are very much elongated and flattened. They contain large amounts of pigment. Just under the fibrous tissue zone many have lost their nuclei and stain poorly. The capillaries are small and often cannot be made out. The portal systems are prominent and the connective tissue about them is markedly increased. Scattered in the liver-tissue there are larger and smaller bands of fibrous tissue. The

smaller bands contain a large number of small round cells and the neighboring liver-cells stain poorly, and many of them have lost their nuclei. In sections that reach the surface of the liver the capsule is seen to be markedly thickened and the compression of the liver-tissue extends throughout the sections. There are no areas of definite necrosis or of abscess-formation in this zone of liver-tissue about the abscess-wall. No amœbæ are to be seen. In some sections where the margin of liver-tissue between the abscess-wall and the surface is thin there are small areas of necrosis of liver-cells to be seen. These areas stain diffusely with eosin, and are composed of a hyaline structureless material. In some places there is a diffuse growth of connective tissue, chiefly in the perivascular spaces along the capillaries between the liver-cells. Here the liver-cells are few, and those remaining form flattened elongated bands. The capillaries contain little blood, but the larger portal ones are congested.

Sections stained in methylene-blue and eosin give a clear picture of the abscess-wall. The granular material in the necrotic zone stains diffusely with the eosin. In places along the inner border there are seen numbers of cells, often in clumps, but here and there scattered cells are seen. The most part of these cells are small round cells with single round nuclei and spindle-shaped cells; but here and there masses of polymorphous nuclear leucocytes are seen. In some places numerous red blood-cells are found. In the necrotic material along the free margin of the abscess-wall and sometimes deeper in the tissue there are numbers of bacteria. The most numerous are short, stout bacilli with rounded ends, lying scattered and in masses. Some longer, thinner bacilli are also seen. These also often lie in masses, usually near the surface of the necrotic layer. Scattered in the necrotic material, usually in the areas of leucocytic infiltration, diplococci are seen. These are less numerous than the other forms. The bacteria in some places are found at the border between the necrotic material and the fibrous tissue zone of the abscess-wall.

In one section the epithelium of a large bile-duct is swollen, desquamated, and the lumen is nearly filled with cells.

In the sections stained with methylene-blue and eosin amœbæ can be clearly made out. They are more numerous in some sections than in others. They are only found in the necrotic layer, and are nowhere in great numbers. They vary in size from 10 to 25 μ . They are usually round or oval in outline. Some are stained deeply with eosin, the nucleus being stained somewhat more deeply than the rest of the organism. Others stain rather diffusely but lightly with methylene-blue, the nucleus being stained a darker blue than the rest. In many of the amœbæ vacuoles are seen. At no place can amœbæ be found invading the fibrous tissue zone of the abscess-wall, and they are not found in the capillaries or veins of the liver-tissue.

Pleura: the changes in the pleura are of a much more active inflammatory character than those met with in the liver-abscess. The pleura is covered with a thick exudation, very rich in fibrin and polymorphous nuclear leucocytes. Some of the cells are broken down and have lost their nuclei. In places there are numbers of deeply staining nuclear fragments to be seen. In sections stained by Weigert's method and in methylene-blue and eosin many bacteria are seen. They are mostly diplococci. Besides these there are short, stout bacilli, and longer

bacilli similar in size and shape to those described in the wall of the liver-abscess. They are met with chiefly on the surface of the exudation. The diplococci can be traced deep into the exudation and reach the pleura proper. At the border between the exudation and the underlying pleural tissues in most places the pleural cells are absent, and the tissue is infiltrated with small round cells and polymorphous nuclear leucocytes. In places the pleural cells have proliferated, and numbers of them can be seen in the deeper layers of the exudation. The bloodvessels of the subpleural tissues are markedly dilated and congested. In the underlying lung-tissue the air-cells are collapsed and their walls lie in juxtaposition. The lung-tissue is congested and here and there are seen masses of pigment. On and near the exudation a few sparsely scattered amœbæ can be made out. They are not found deep in the exudation or near the pleura. None can be found in the lung-tissue.

Pericardium: sections made from the pericardium over the surface of the right ventricle, and stained with methylene-blue and eosin, show the presence of a fibrinous exudation. In this there are not a great number of leucocytes. The bloodvessels of the endocardium are deeply congested. In the exudation large numbers of cocci are seen. Besides, there are a few long bacilli and some short, stout bacilli. In places the lining cells of the epicardium are swollen and desquamated. In the exudation, besides these cells, there are larger ones, staining like the amœbæ in the liver-abscess and of the same size and appearance. They can be distinguished from the epicardial cells by their size, the presence of larger and smaller vacuoles, and the difference in their nuclei. They are fairly numerous. The epicardial cells are smaller, have no vacuoles, and have larger, rather oval vesicular nuclei.

In the hardened specimens no special changes are seen in the heart-muscles.

The kidneys show well-marked chronic passive congestion and slight chronic diffuse nephritis. The spleen is markedly congested.

PATHOLOGY. In considering the pathological anatomy of tropical abscess of the liver, we will deal first with that form associated with previous or existing dysentery, and then with the so-called "idiopathic" liver-abscess. We shall leave out of consideration entirely the metastatic liver-abscesses following typhoid and tuberculous lesions of the intestinal tract, catarrhal and croupous dysentery, peritonitis, appendicitis, and perityphlitis, and pyelitis of the portal vein, suppurative endocarditis and the like. All these varieties are usually seen as multiple small abscesses, and are quite distinct in their etiology, size, situation, and anatomical appearances from the tropical abscess.

The form of dysentery followed by liver-abscess is peculiar, etiologically and anatomically. It is characterized by the formation of larger and smaller ulcers, usually deep, with irregular overhanging edges. In many places, in addition to the ulcerative process, larger and smaller abscesses exist in the submucosa under an apparently intact mucosa. In some places these communicate with the lumen of the intestine by small openings, through which puriform material can be squeezed. In some cases the muscularis is extensively invaded, and perforation may

result. In the more severe cases there are long sloughs involving the mucosa, submucosa, and muscularis. Kartulis, Councilman and Lafleur, and Kruse and Pasquale, especially, have identified this alterative form of dysentery with the tropical dysentery and have established the etiological relation of the *amœba coli* to it. These authors and others have found this organism invariably associated with the lesions in a way that leaves no doubt that it is the cause of the ulcerative process, which may be and usually is modified by the presence of various bacteria which mark the ulcers secondarily. The *amœbæ* penetrate the mucosa and seek the submucosa. They may sometimes be found in the intestinal glands. The primary changes are in the submucosa. The mucosa is affected secondarily. Abscesses of varying size are found in the submucosa, and may burrow for considerable distances without breaking through the mucosa or invading the muscularis. Usually, however, both of these coats are finally involved in the process. *Amœbæ* are present in large numbers in these abscesses and in the ulcers. The changes are usually limited to the colon, but not uncommonly the rectum, cæcum, and even the ileum for a short distance are involved. The tissue-changes are chiefly those of necrosis and liquefaction. The *amœbæ* are abundant in the lesions, and may be found for some distance away penetrating into the neighboring tissues.

The proportion of cases of this *amœbic* dysentery complicated with liver-abscess varies within rather wide limits in the experience of individual observers. The statistics collected by Councilman and Lafleur show that in India in 1429 autopsies on individuals dying of dysentery, liver-abscess occurred in 306, or one case of liver-abscess to every four and one-half cases of dysentery. In Algiers, of 1001 autopsies on dysentery cases 180 had liver-abscess, or a proportion of one liver-abscess to five of dysentery. According to Kartulis, of 500 cases of dysentery, from 50 to 60 per cent. had liver-abscess. Of 40 American cases collected by us, 18 had liver-abscess. Liver-abscess may occur in the acute form of dysentery, but it is more common in the chronic variety, and then its course is often so insidious that clinical symptoms are lacking until the abscess is large or even ruptures.

By far the most common seat for these abscesses is in the right lobe of the liver. When the left is affected, it is usually in conjunction with the right. They are usually situated in the upper portion of the right lobe of the organ, just beneath the diaphragm. Next in frequency comes the lower portion of the right lobe, corresponding to the hepatic flexure of the colon. Kruse and Pasquale describe in one case an abscess in the lobus quadratus. The abscesses may start near the surface or deep in the hepatic tissue. They are more commonly single, but may be multiple; rarely, however, are there more than two or three. Occasionally they are small and numerous, widely distributed through-

out the organ, and affecting both the right and the left lobes. In some cases several small abscesses may be grouped about a large one. Sometimes two or more abscesses may be connected by sinuses.

In size the abscesses vary from microscopic points to large collections of pus occupying as much as two-thirds or more of the liver-substance.

The abscess-contents consist usually of a reddish-brown, anchovy-sauce-like material, which is in some cases of an almost gelatinous consistency. In other cases the material is of a grayish-white appearance and contains larger and smaller masses of necrotic tissue.

The abscess-walls are usually ragged and show larger and smaller, irregular, soft, grayish masses of necrotic material. When the process is of recent date the abscess-wall is soft and the line of demarcation between it and the liver-tissue is irregular. In the older abscesses, beneath the soft necrotic material, there is usually a layer of rather translucent gelatinous-like material of varying thickness. Beneath this, and separating it from the surrounding liver-tissue, there is a zone of fibrous tissue which in old abscesses is dense and firm. This zone varies very much in thickness. In these abscesses the necrotic zone is often narrow and the fibrous tissue layer is thick. Always beneath the fibrous tissue zone the surrounding liver-tissue is compressed and indurated. Not infrequently scars of healed abscesses are found in the livers of individuals who have had dysentery, and die long afterward of some other affection.

Livers the seat of abscesses vary very much in size. Often the organ is not at all enlarged, and it may even be smaller than normal in cases of chronic abscess in the process of healing. Often the abscess or abscesses just fill the space of the degenerated and necrotic liver-tissue. In other cases the liver is enormously enlarged, usually in the case of multiple abscesses. In chronic abscesses the size of the liver or of the affected lobe is often much decreased, due to the absorption of the purulent material, and the focal and diffuse cirrhosis that follows. The more fluid portion of the abscess-contents is composed almost entirely of granular detritus, and few well-preserved cellular elements are found. In recent abscesses degenerated granular and fatty liver-cells may be seen; in the pus from older abscesses these are usually absent. Rarely are polymorphous nuclear leucocytes found, and when present they are very few in number, and usually there is a bacterial mixed infection. Red blood-corpuscles are commonly seen, both well preserved and in various stages of degeneration. Careful search, which, however, in some cases must be repeated, practically always discloses amœbæ. Often they are missed in aspirated pus, which probably usually comes from the central and older part of the abscess.

In even the smallest abscesses Councilman and Lafleur found amœbæ. According to their studies, the tissue-cells undergo necrosis and finally

become liquefied, and this is probably associated with a serous exudation from the bloodvessels. There is a striking absence of nuclear fragmentation. In some cases they describe a necrosis of liver-cells in which the cells preserve their form, while in others they are broken up into highly refractive masses, and in still others they appear as fragments lying between the capillaries. These changes were noted in all of their cases, were not associated with the presence of amœbæ, and were best marked in an acute case. These changes were met with always in the central portion of the lobule, and were often confined to a few cells near the central area. They showed no leucocytic invasion, and were not associated with the complete liquefaction of tissue and the formation of abscesses that occurred when amœbæ were present. These authors attribute these diffusely scattered areas of necrosis of liver-cells to the action of soluble toxic substances produced by the amœbæ in the intestinal lesions, and absorbed and then brought to the liver, while the necrosis and liquefaction of tissue in the abscess-areas are due to the direct action of the amœbæ themselves.

They point out that these focal areas of necrosis may lead to cirrhosis of the parts of the liver affected, as sometimes occurs in India as a sequence of dysentery.

The small abscesses may be microscopical in size. They vary in shape, and their contents consist of firmly granular material with here and there cellular and nuclear fragments, and in some there is fibrin. Few, if any, leucocytes are seen, but red blood-corpuscles may be numerous. In the larger abscesses there may be more solid masses composed of liver-tissue that has escaped destruction. Often these masses represent portal systems, the interportal tissue having liquefied. Amœbæ are always numerous in the smaller abscesses, being more numerous about the periphery, extending in places into the liver-tissue, but not usually beyond the area of tissue-necrosis. A few may be found in the capillaries. The smaller abscesses do not exert any pressure upon the surrounding tissue. Abscesses of microscopic size may be found in every way connected with the larger abscesses.

In the larger and older abscesses generally three zones can be made out: an inner necrotic granular zone, then a highly refractive reticulum, and outside of this a layer of granulation-tissue of varying thickness. The appearances described in Case IV. are quite characteristic. The inner necrotic zone shows granular detritus, a few or more small round cells, few or many red blood-cells, and sometimes polymorphous nuclear leucocytes. Sometimes necrotic and fatty liver-cells are present. Usually in this zone amœbæ can be made out. They vary very much in number. Some sections may contain many, while in others few or none are seen. A striking thing in most cases is the absence of polymorphous nuclear leucocytes.

The granulation-tissue of the outer zone may be markedly cellular, but in the older abscesses the cells are few in number and those present are, for the most part, spindle-shaped.

Bile-ducts lined with cuboidal epithelial cells are numerous about and often in this layer. The bloodvessels are dilated, but often the walls of the capillaries are thickened. At the margin of the fibrous tissue zone the liver-tissue is compressed, and the liver-cells, being spindle-shaped, often lie in long, flattened rows. The connective tissue of the perivascular spaces is increased, many of the capillaries are obliterated, and the central areas have disappeared. The bile-ducts are numerous in some places and absent in others. There is a more or less well-marked cirrhosis of the liver-tissue, then, for a varying distance from the abscess.

There is a striking difference between the appearances, both in the acute and in the chronic amœbic abscesses, from those met with in abscesses due to bacterial invasions. In the amœbic abscess there is a striking absence of leucocytic reaction, and both the amœbæ and their toxic products evidently lack positive chemotactic properties for leucocytes, or even exert negative chemotaxis on these cells. In the amœbic abscess with bacterial mixed infections the difference in the number of leucocytes present is marked. In general, it can be said that pus with few or no leucocytes coming from a liver-abscess is of amœbic origin. If, however, there is a bacterial mixed infection, numbers of leucocytes may be present, the organisms causing the mixed infection being the cause of the leucocytic invasion.

Liver-abscesses may communicate with various organs and cavities. The most common secondary invasion is undoubtedly through the diaphragm into either the right pleural sac or directly into the lower lobe of the right lung.

If the communication here is due to a sudden rupture of a liver-abscess through the diaphragm, or, as may also occur, a rapid extension of the amœbic microbe process through this organ, the pleura rather than the lung is affected.

The opening of a liver-abscess into the lung, and the extension of the process into this organ, more commonly take place when the process gradually extends through the diaphragm and there is time for the occurrence of an adhesive inflammation between the visceral and diaphragmatic pleura. In the former case there is a sudden rupture through the diaphragm, with the evacuation of a large amount of pus into the pleural sac, with retraction of the lung. The pleura soon becomes thickened and covered with a ragged, easily broken-down necrotic material similar to that lining the liver-abscess. The retracted lung becomes firmly bound down by the thickened pleura, the thickness of which varies greatly. The pleural reaction in these cases usually protects the lung from invasion, and a pneumothorax rarely occurs.

When the process from the liver-abscess invades the lower lobe of the right lung the resulting abscess shows very much the same appearances met with in the liver. The histological changes are, according to Councilman and Lafleur, much the same. The changes in the interstitial tissue are, however, more marked in the lung than in the liver, and there is usually a well-marked chronic interstitial pneumonia, the reaction being on the part of the interstitial tissue of the alveolar walls. The same degeneration and liquefaction of tissue are met with in the lung as in the liver. Abscess-formation is usually confined to the lower lobe, and the abscesses are usually single, but may be multiple. The lung-abscesses usually open into one or more bronchi, and the hepatopulmonary abscess is thus drained. One of us has twice been able to make a diagnosis of unsuspected hepato-pulmonary abscess from an examination of the sputum; in both cases amœbæ were present in large numbers and were by far the most numerous cells in the sputum.

The lung is rarely, if ever, infected with amœbæ by the circulation. If amœbæ are carried from the liver by the hepatic vein—and it is difficult to see why this must not uncommonly happen—they certainly do no harm. Rarely, liver-abscess may rupture into the vena cava, and a large amount of pus may be carried to the lung, but death occurs before multiple abscess can form.

The pericardium may be invaded in two ways: (*a*) by the opening of a liver-abscess directly into the pericardium, and (*b*) by extension from either the pleural cavity or from a lung-abscess, either by rupture or by the gradual extension of the process through the pleura and pericardium, of which Case IV. is an example. A sinus may connect the two cavities. The character of the pus found in the pericardial cavity will depend upon the source of the pus: whether it is from the liver, the pleura, or the lung; upon the length of time the pericardium has been affected; and upon the presence or absence of a bacterial mixed infection. In our case with mixed infection there was a marked inflammatory reaction, with the presence of a number of leucocytes in the pus. Amœbæ have not, so far as we have been able to learn, been described in the pericardium. In Case IV. they were found in the fresh pus, in the necrotic material covering the pericardium, and in the sections of the hardened tissues.

Hepatic abscesses may rupture into the gall-bladder and discharge their contents into the duodenum, or they may rarely rupture into the stomach.

Rupture into the abdominal cavity occurs but rarely. The right kidney may form a part of the wall of a liver-abscess and the pus may discharge in the urine.

Thierfelder collected 170 cases of liver-abscess, of which 76 opened into the lung and bronchi, 23 into the abdominal cavity, 32 into the intestine, and 13 into the stomach.

Aghetti collected 131 cases, of which 38 broke into the lung.

Three of our cases opened into the right pleural cavity. By far the most common place for rupture of hepatic abscess is into the thoracic cavity.

In four cases in which the heart-muscle has been examined (three cases by Flexner and our own case, IV.) fatty degeneration has been found. The changes in the kidney are limited to cloudy swelling and fatty degeneration, except in the rare cases where the right kidney forms a part of the wall of a liver-abscess. The spleen is usually enlarged, and is sometimes soft and sometimes firm, the latter usually being dependent upon a long-standing passive congestion. In one case of liver-abscess Krause and Pasquale found small pus-collections in the spleen distributed along the branches of the splenic veins. They think that this was brought about by the backward flow of pus which gained access to the portal vein.

Councilman and Laffeur failed to find the focal areas of necrosis in other organs than the liver. They were not present in our case.

The peritoneum may be invaded in several ways. In a few cases there is a peritonitis starting from the peritoneal coat of the intestine corresponding to the seat of the ulcers. The exudation is sometimes abundant, is of a peculiar gelatinous consistency, and contains large numbers of amœbæ. Bacteria may or may not penetrate the intestinal walls in these cases. If a liver-abscess ruptures into the peritoneal cavity, there is a widespread peritonitis with pus of the same character described above. Chronic fibrous peritonitis with thickening over the ulcers in the intestine is not uncommon. Chronic adhesive peritonitis about the liver, between the organ and the diaphragm, abdominal wall, omentum, and the transverse colon is common.

The macroscopical appearances of the so-called "idiopathic" liver-abscess are described as being similar to those of the chronic abscess associated with dysentery. They usually have firm fibrous walls.

So far as we can learn, there is no account of the histological lesions and no good description of the process. The histological study of the process in these cases promises much in clearing up their etiology.

The amœba coli, described first by Lösch in 1875, in the stools of an individual with dysentery in St. Petersburg, has since been found in dysenteric discharges, in the pus of liver- and lung-abscesses, and in lesions of the colon, liver, lung, and pleura; in cases in Egypt by Kartulis (1885-1891), Koch (1887), and Krause and Pasquale (1893); in Russia, by Massiutin (1889); Bohemia, by Hlava (1887), Kovacs (1892), Epstein (1893); in Gratz, by Cohen (1891); in Italy and Sardinia Calaudruccia, and by Fenaglio (1890); in Baltimore, by Osler, Löffler, Simon, Councilman and Laffeur, Howard, Thayer (1890-1893); in Texas by Dock (1891); in Philadelphia by Musser and

Stengel (1890); in Cincinnati by Eichberg (1891); in Alabama by Wilson (1895), and by others in America; in Germany by Nasse (1892), and Quincke and Roos (Kiel, 1893); in Greece by Kartulis (1890); and in Brazil by Lutz (1891).

As far as we can find, amœbæ have not been looked for in the dysenteric and liver-abscess of India, though they have been found in liver-abscess in England, occurring in returned East Indians (Mason and Galloway).

The amœbæ described by Lösch varied in diameter from 8 to 37 μ , and had one or two blunt pseudopodia. The ectosarc was apparent only in the resting stage; the endosarc was firmly granular and contained small non-contractile vacuoles, besides red blood-corpuscles, intestinal epithelium, and fecal particles. There was a vesicular nucleus of from 5 to 7 μ in diameter.

The chief difference between the amœba of Lösch and the amœbæ described by later authors is one of size, the latter being uniformly larger—from 10 to 50 μ in diameter. Kartulis has described "giant amœbæ" measuring from 150 to 222 μ in diameter. Certain other differences have been noted by various observers. Kartulis, Osler, Councilman and Lafleur, and Kruse and Pasquale have given very accurate descriptions.

According to Councilman and Lafleur, when inactive, the amœbæ are round or slightly oblong and more refractive than the other cells in the containing discharges. While at rest there is usually no distinction between the ectosarc and the endosarc, but the organism has simply the appearance of a body enclosing clear, pale vacuoles of varying size, which vary from bodies a third the size of the organism to tiny vacuoles. When the organism sends out pseudopodia the ectosarc appears as a pale, hyaline, homogeneous substance, less refractive than the inner substance.

Nearly all observers have noted two kinds of motility—a progressive movement which is slow and a movement characterized by the pulling out and retracting of pseudopodia. An amœba may suddenly put out and retract large pseudopodia, and then remain quiescent. This may be repeated at varying intervals. In others the movements are slow and prolonged. A very irregular contour of the organism is produced by the putting out of several pseudopodia at the same time. The pseudopodia are always blunt, and they have the same hyaline appearance of the ectosarc, and in some instances are very long. Often the contents of the amœba rapidly flow into the protruded part and change of place occurs. The nucleus is made out with difficulty in the first state, being often obscured by the large vacuoles. The nucleus does not stain with methylene-blue, but will stain well with acid fuchsine, safranin, and eosin. Councilman and Lafleur obtained the best results with sections

hardened in Flemming's solution and stained with safranin, but also obtained good results from alcohol sections stained with methylene-blue. They found that the nucleus lies near the surface at the edge of the endosarc, is vascular, disk-shaped, and about the size of a red blood-corpuscle. These authors do not think that the endosarc is granular, but that this appearance is given it by the presence of very small vacuoles.

The amœbæ often contain foreign bodies, such as red blood-corpuscles, either well preserved or in various stages of disintegration, leucocytes, small round cells, epithelial cells, hepatic cells, nuclei of broken-down cells, blood-pigment, micrococci, bacilli, and spores.

Kruse and Pasquale distinguish four varieties of amœbæ in stools:

a. A form with poorly differentiated endoplasm, with small scattered granules, and very highly refractive, which distinguishes it from the ectoplasm. This form is found in normal feces.

b. Amœbæ with highly granular endoplasm, the granules being very irregular in size, but usually small. This form they found only uncommonly in dysenteric stools.

c. Amœbæ, the endoplasm of which is apparently a conglomeration of larger and smaller vacuoles. This form they found most common in dysenteric stools.

d. Amœbæ with endoplasm containing many foreign bodies, as red blood-corpuscles, leucocytes, bacteria, pigment, etc.

They describe the nucleus, in the amœbæ of normal as well as that of the dysenteric stools, as being about the size of a large vacuole, with an average diameter of 6 μ . They note two modes of multiplication, division and sporulation, but were able to prove neither way for amœbæ of either normal or dysenteric stools. They describe an encysted stage, and were able to infect cats with this form.

Amœbæ have been found in the stools of healthy persons by Grassi, Kruse and Pasquale, and Shuberg, as well as in the stools of persons with various intestinal diseases, as typhoid fever, cholera, pellagra, colitis (Grassi, Cunningham). Kruse and Pasquale found numbers of amœbæ in the stools of healthy persons, including their own, in Naples, but rarely in Egypt.

Shuberg found amœbæ in the stools of twenty healthy persons after the administration of Carlsbad salt, but never after castor-oil, which he thinks must exert a harmful action on these organisms. Shuberg's explanation of the occurrence of amœbæ in the stools after taking the salt is that the usual acid reaction of the intestine is in this way modified, or rendered alkaline, thus favoring the growth and multiplication of amœbæ which may be taken in food and water, but which are usually killed by the ordinary acid reaction of the colon.

Kruse and Pasquale were unable to find any constant morphological differences between the amœbæ of normal and dysenteric stools, except

that the amœbæ found in the latter caused colitis with ulceration in cats, while those in the former were harmless for these animals.

Quinke and Roos have carefully studied the amœbæ found in two cases of dysentery. In the stools of the first case they found rather small amœbæ (20 to 25 μ) with rather finely granular protoplasm and round nuclei. The amœbæ-containing stools of this case when introduced per rectum were pathogenic for cats, the animals dying in from two to three weeks with an ulcerative inflammation of the large intestine. Amœbæ introduced per os were harmless, while encysted forms introduced by this channel caused dysentery in cats.

In their second case the amœbæ were from 25 to 30 or 40 μ in diameter, were coarsely granular, contained many vacuoles and foreign particles, but no red blood-corpuscles, and were less actively motile than those of the first case. Encysted forms were also seen. Repeated injections of the stools of this case caused a diarrhea without anatomical lesions in cats. These authors repeated Shuberg's experiment upon twenty individuals, some healthy and other patients in the medical clinic. Amœbæ were found in the stools of nine, but were numerous in only three cases, and were not pathogenic for cats. Based on these observations, Quinke and Roos make three classes of amœbæ parasitic for men :

1. Amœbæ intestini vulgaris, 40 μ in diameter, with large granulations ; pathogenic for neither men nor cats.

2. Amœbæ coli mitis, of about the same size and appearance as the above ; pathogenic for men, but not for cats.

3. Amœbæ coli Lösch, or amœbæ coli felis, about 25 μ in diameter, finely granular, and producing dysentery in both men and cats.

Kartulis (1891) first produced dysentery in cats by rectal injections of amœbæ-containing stools. He also claims to have cultivated amœbæ from dysenteric stools in straw-infusion, and to have produced the disease in cats by rectal injections of these amœbæ. No one has so far been able to repeat these experiments. The attempts of Kruse and Pasquale to cultivate amœbæ from stools were unsuccessful, and they think that Kartulis was dealing with the amœbæ of straw-infusion, and not with dysenteric amœbæ.

Kruse and Pasquale produced well-marked inflammation of the colon, with ulceration, in cats by rectal injections of the amœbæ-containing dysenteric stools, and also of amœbæ-containing, but bacteria-free, pus from a liver-abscess. Numbers of amœbæ were found in sections of the hardened tissues. These authors found the amœbæ-containing stools of healthy persons harmless for cats. They think that the only way in which a positive diagnosis between the pathogenic and the harmless intestinal amœbæ can be made is by animal experiment.

Braun, in a careful review of all the observations on the subject, considers that there are two specific kinds of amœbæ for men and cats, the

one with fine granulations, which is pathogenic; the other, coarsely granular, is harmless. He does not think that the pathogenic amœbæ are infectious *per os*, but that the encysted forms are.

Amœbæ have been described as being present in the human mouth by Gros, Sternberg, and Grassi. In 1883 Baelz described amœbæ 50 μ in diameter in the bloody urine and in the vagina of a woman with vesical tenesmus. In 1889 Jürgens found amœbæ in a case of mucous cysts of the bladder. Kartulis found amœbæ from 12 to 20 μ in diameter in the urine of a man with tumor of the bladder. In 1893 Pasner described amœbæ in the urine of a man with hæmaturia. Flexner has described amœbæ indistinguishable from the amœba coli in the pus from an abscess of the jaw. Kartulis has reported a somewhat similar case from Alexandria. Nasse has described amœbæ in the gangrenous skin and muscle of the chest in a man operated on for amœbic abscess of the liver.

Of all those who have attempted to cultivate the amœbæ coli, until very lately, Kartulis alone has reported positive results.

In 1894 Celli and Fiocca reported that they had succeeded in cultivating amœbæ from the intestinal contents of healthy men and of men with different intestinal diseases, from the vaginal and buccal secretions and from the intestines of animals, and in waters from various sources, upon a special culture-media devised by them; amœbæ failed to grow in the ordinary laboratory media. They did not describe the media they used.

They conclude from their studies that all amœbæ have two stages, the amœboid and the encysted. In the encysted stage the contents of the organism are more or less granular, and are included in a double-wall capsule, the inner wall of which is smooth, the outer being either smooth or wavy, so that the contour of the cyst may be either smooth or wrinkled. In the amœboid stage the endoplasm they describe as being granular, while the ectoplasm is hyaline. A vesicular nucleus and from three to seven vacuoles can usually be made out. The amœbæ feed on solid bodies, especially bacteria and their spores, and break up red blood-corpuscles without setting free the pigment.

Multiplication was always by division, and they failed to observe sporulation.

In hanging-drop preparations of encysted forms, in most cases in from two to six hours, the contents of the encysted forms became granular, the nucleus apparent, and the organism motile. In a variable time, through a break in the cyst-wall, the organism is discharged, and, after clinging for a short time to the side of the cyst, is set free as a young amœba. In a short time this will divide, and amœbæ rapidly multiply. This process usually lasted from twenty-four to seventy-two hours. In some forms encapsulation begins after twenty-four hours, and in others

after forty-eight or seventy-two hours. After from three to seven days the outer wall takes on a round or wrinkled contour. After a certain time, if these amœbæ were placed in a new medium, the cycle began again. In certain cases, however, involution-forms, very finely granular, more or less round, and with wrinkled contour, were observed. According to these authors, both the amœbæ and the encysted forms can resist without dying a temperature of from 0° to 15° . In the amœbic stage they die of exposure to a temperature of 45° for five hours, or 50° for one hour. In the encysted stage they can bear 60° for one hour, or 55° for four days, and for seven days a temperature of 67° for several hours a day. They withstand more or less rapid drying in either diffuse light or in darkness. They withstand sunlight in dry or damp substances for 270 hours at a temperature of from 12° to 15° .

Amœbæ would not grow in anaërobic cultures, although they may be found two metres below the surface of the ground. In putrefying animal fluids amœbæ die after twenty-three days, encysted forms after thirty-three days. Both amœbæ and encysted forms were killed by the action of various chemicals, as soon as the bacteria that were with them; more quickly by acid than by alkaline solutions, however.

They were not able, either by chemical or by mechanical means, to obtain bacteria-free cultures of amœbæ.

In a later article Celli and Fiocca, based upon their studies by culture-methods and otherwise, classify amœbæ obtained by them from various places, including the normal and dysenteric stools, stools from cases of intestinal catarrh, the intestines of animals, from the water of wells, springs, river, swamps, and from the ground and from dust. In dysenteric stools, besides the *amœba coli*, they found other forms (*A. spinosa*, *diaphana*, and *reticularis*). Some of these organisms were found in the contents of the normal intestine as well as in cases of intestinal catarrh, and even in the vagina. According to these authors, amœbæ may be carried from the ground to the air in dust. Amœbæ were not found in the mouth or pharynx, nose or ear.

They describe four varieties of amœbæ *lobosa*, and place the *amœba coli* Lösch under this head. In all they describe five species, and they give descriptions and cultural characteristics of these, but do not describe the media they used.

In January of the present year Beyerinck described two varieties of amœbæ cultivated by him upon solid media. He found that a peculiar earth amœbæ grew upon a special media made with agar, which he used for the study of the bacteria of nitrification. He gives full directions for making this media, for which the reader is referred to his article. Upon the surface of his agar-plates this peculiar spore-formation amœbæ grew rapidly, the colonies appearing first as small granular points on the surface, and from these the growth in some cases spread all over the

surface of the plate. The amœbæ in this manner followed distinctly the colonies of the earth bacteria which grew in the culture, feeding upon these organisms. The amœbæ cultures were best transferred by inoculating them upon an agar-plate which had already a growth of earth bacteria. In this case the amœbæ multiplied, feeding upon the bacteria. He gives an interesting description of this organism, which he calls *amœba nitrophila*, and finds it very common in garden earth.

Later, on making cultures from some fermenting grapes, he found, besides *saccharomyces apiculatus*, a peculiar dimorphous glucose-yeast and an acetic-acid bacterium, a form of amœbæ which he thinks was perhaps identical with *amœba coli* Lösch. The medium used in this case was malt-extract gelatin. He gives a most interesting account of the modes of growth and of the cultural characteristics of this amœba on malt-extract gelatin, beef-peptone gelatin, on agar, and on his nitrification media.

The organism multiplied rapidly, growing both in separate colonies and as a spreading, veil-like growth over the surface of the media and under a variety of conditions. It would grow well with the *apiculatus*, or with the acetic-acid bacterium, or with both, using either or both these vegetable forms as food. An interesting phenomenon was the liquefaction of the gelatin, which occurred in all gelatin-cultures, but most especially well marked in malt-extract gelatin. It was better marked in cultures of amœbæ plus *apiculatus*, with a neutral or alkaline reaction, than in cultures with the acetic-acid bacterium.

This peptonization of the gelatin he thinks is due to an enzyme set free from the amœbæ as a waste-product, not by simple diffusion, but through the vacuoles, and that this enzyme is trypsin. It is free from diastase, glucose, and invertase. This amœba, which he calls *amœba zymaphila*, has a nucleus. There are no pulsating vacuoles and no "neben-vacuolin," as in his *amœba nitrophila*.

Spore- and cyst-formation were not observed, and multiplication took place by simple division.

In a third article Celli gives his method of cultivating amœbæ upon solid media. He succeeded in getting a scanty culture upon alkalized potato, ascitic fluid, and egg albumin. He got good results with *fucus crispus* made up like agar, 5 per cent. in water, with or without bouillon, and rendered strongly alkaline. In this medium he obtained pure cultures of different varieties of amœbæ, including the *amœba coli*.

Schardinger has cultivated various protozoa on gelatin and on hay-infusion agar, on the latter medium obtaining cultures of the *amœba coli* from the stools of a patient with dysentery. He describes an encysted stage, and was able to grow amœbæ from this.

These observations and the ability to cultivate amœbæ on solid media promise much in the near future in the study of the etiology of pro-

tozoan infections. The enzyme-producing amœbæ of Beyerinck is of peculiar interest. As Councilman and Laffleur point out, there are focal areas of cell-death not associated with the presence of amœbæ, occurring in the liver in cases of amœbic dysentery, which they suggest is due to the action of soluble toxins produced by the amœbæ in the intestinal lesions. This observation of Beyerinck is a valuable confirmation of their interpretation of the process. It also suggests that the cell-destruction and liquefaction of the tissues in the amœbic processes may be due to the action of this or of a similar ferment.

Bacteria are not uncommonly associated with amœbæ in the liver- and lung-abscesses, as well as in the intestinal lesions.

Kartulis, in cultures from thirteen cases of liver-abscess, found bacteria in five, the staphylococcus pyogenes in two, the staphylococcus pyogenes albus in one, the bacillus pyogenes foetidus in one, and the proteus vulgaris in one.

Councilman and Laffleur found bacteria in the sections from liver-abscesses in three of six cases, but obtained positive results by culture-methods in only one case—the colon-bacillus. They call attention, however, to the presence of bacteria in the intestinal lesions, where these organisms may modify to a greater or less degree the lesions caused by the amœbæ.

In seven cases of liver-abscess associated with dysentery, in Egypt, Kruse and Pasquale found streptococci in three cases and staphylococci in two. With these there were often found "typhoid-like" bacilli (colon-bacilli?) and streptothrix. In cultures made from dysenteric stools they found streptococci the predominant organism. In three cases dead of amœbic dysentery they found streptococci in the liver, and in one of these in the mesenteric glands and in the portal vein. In a fourth case streptococci were found in the mesenteric glands. In Case IV, we found in the liver-abscess and in the pleura and pericardial exudations the staphylococcus pyogenes aureus, the colon-bacillus, and a long, unidentified bacillus.

Flexner has found streptococci in small abscesses of the liver in a case of amœbic abscess of the liver, with perforation of the vena cava and hemorrhage into the abscess. No amœbæ were found in the small abscesses, but in the large abscesses there were amœbæ and a variety of bacteria. All these authors regard the presence of bacteria in this variety of hepatic abscess as secondary invasions, mixed infections, and as bearing no etiological relation to the primary lesion. The presence of bacteria in the intestinal lesions is to be regarded in the same light.

While careful search practically always demonstrates the presence of amœbæ in the secondary liver, lung, and pleural abscesses occurring during the course of or following amœbic dysentery, very little is

known of the etiology of the so-called "idiopathic" abscesses of the liver; that is, in those cases in which the process is apparently primary in the liver and not secondary to intestinal lesions.

So far as we can learn, amœbæ have never been demonstrated in this form of liver-abscess. In the cases examined bacteriologically by Kartulis, the staphylococcus pyogenes was found in four and the staphylococcus albus in one; the remainder were sterile.

In seven cases Kruse and Pasquale found the bacillus pyocyaneus in two, the staphylococcus pyogenes aureus in one, the staphylococcus in one, and typhoid-like bacilli in one. None of their cases came to autopsy, the pus being obtained by aspiration or at operation.

There are many reasons which make it seem probable to us that certainly a large proportion, if not all, of these abscesses are caused by the amœba coli, or at least by a similar organism. No constant variety of bacteria is found in them, and the form of reaction, so far as we know it, points to their amœbic origin. The characters of the pus in the two varieties is described as being the same. As is well known, in cases of amœbic abscess of the liver associated with a previous or with an existing dysentery, amœbæ may be very scarce or even entirely lacking in the pus, especially if the process is an old one, and the walls are firm and fibrous and the pus is obtained by aspiration. One of us has observed this repeatedly. In all the cases of idiopathic abscess reported by Kruse and Pasquale these conditions evidently obtained—the pus was obtained either by operation or aspiration.

The walls of the abscess were not examined for amœbæ, and it cannot be positively stated that they were absent.

In both varieties the pus is described as being very much the same, usually anchovy-like in color and consistence, poor in cells, especially in leucocytes, and consisting chiefly of granular detritus. The absence of leucocytes points more decidedly to the amœbic than to the bacterial origin of the idiopathic abscess.

There is absence of a history of primary suppuration elsewhere, and the seat of the abscess is very constantly the same as that of the dysenteric form. In the two varieties, bacteria, usually the pus-cocci and the colon-bacillus, are found in about the same proportion of cases, and their presence can be explained as secondary mixed infection in the one case as in the other.

As pointed out by Kartulis, Councilman and Lafleur, and Kruse and Pasquale, in the amœbic dysentery the amœbæ are in the intestinal glands, about the ulcers, in the mucosa, and in the submucosa. They are found not infrequently in the veins, and in some cases they certainly penetrate the intestinal walls and reach the peritoneal cavity. Councilman thinks that the organism most commonly reaches the liver by means of the peritoneal cavity, by passing through the intestinal walls,

and that once in the cavity they are carried, as are other foreign particles, up behind the liver. He does not regard with favor the idea that they reach the liver by means of the portal vessels. We must, however, regard the latter as the most probable channel of infection for the liver, both in the large, deep-seated abscesses, as well as in the widespread multiple small abscesses, which are all of about the same age and size. It is extremely improbable that amœbæ ever reach the liver by way of the lymph-channels, on account of the barrier offered by the lymphatic glands. Kruse and Pasquale suggest that amœbæ may reach the liver by the bile-duct and the bile-tract. This would explain the mode of origin of many of the so-called idiopathic abscesses.

It is not impossible that at least some cases of the idiopathic liver-abscesses are caused by amœbæ that have penetrated to the submucosa of the intestine possibly through small breaks in the mucous membrane or even through the unbroken mucous membrane, causing only slight local lesions, and, getting into the lumen of small veins, may reach the liver. Here, under more favorable conditions, possibly, than exist in the intestine, they may multiply and cause abscesses, while the process at the infection-atrium heals. Another possibility is the presence of one or more small amœbic ulcers in the rectum, colon, or cæcum, or even the small intestine or the stomach, which are too small and insignificant to cause diarrhœa or other symptoms. It is also very significant that the "idiopathic" liver-abscess is most frequently met with in those countries and in those conditions in which the dysenteric liver-abscess is most common. There are numerous analogies in the pathology of the infectious diseases which support this explanation of the etiology and mode of origin of the idiopathic liver-abscess.

CLINICAL HISTORY AND DIAGNOSIS. Tropical abscess of the liver may run its entire course without giving any subjective symptoms that would attract the physician's attention to the liver, and, indeed, without causing the patient any great degree of suffering until shortly before the fatal termination.

Rouis says 15 per cent. and Chyostek says 25 per cent. of the cases are painless. Sachs¹ aspirated one and one-half quarts of pus from an hepatic abscess that had caused neither pain nor great inconvenience of any kind. Fayrer² reports a case of a young man in India, aged twenty-two years, who had slight chills simulating malaria; he also had diarrhœa and was anæmic. The liver was large, not sensitive to pressure; no pain whatever. This condition lasted about six months, when one day, while boxing, he received a blow in the right hypochondrium, vomited a large amount of pus, and subsequently recovered his health.

¹ Sachs: *Gaz. hebd. de méd.* Paris, 1868, v. p. 214.

² Fayrer: *Brit. Med. Journ.* London, 1874, ii. p. 401.

A. S. Adams¹ reports a case of a young soldier in India who died twelve days after admission to the hospital. He suffered no pain nor uneasiness in the liver region. The autopsy revealed a large abscess occupying the right lobe and another abscess occupying the left lobe of the liver, leaving only one-quarter of an inch of hepatic substance surrounding them.

Haspel (referred to in Bertrand and Foran's work) reports the case of a young soldier in the tropics who, suffering no inconvenience on the march, suddenly fell down and died in great agony from suffocation. A large abscess of the right lobe of the liver had broken into the right thoracic cavity.

Rouis reports the case of a soldier who had constantly reported for duty. The man was killed in a street row. The autopsy revealed a large abscess in the right lobe of the liver. Another case reported by Borius was that of a young soldier on the march in India, who died suddenly while kneeling down drinking from a spring at the roadside. At the autopsy it was found that a large abscess of the liver had ruptured into the peritoneal cavity.

It is also rather surprising that vomiting, icterus, and ascites are not more frequent accompaniments of the tropical abscess. The absence of vomiting is explained by the location of the abscess in cases originating from the *ameba coli*. The tropical abscess is located in the vast majority of cases at the superior and posterior portions of the liver, whereas vomiting is a frequent occurrence when the abscess is located in the posterior and inferior regions or in the lobus *Spigelius* or *quadratus*.

Absorption-icterus is rare in tropical abscess because of the location and manner of growth of the abscess. In the cases of abscess of portal origin icterus is relatively more frequent, and even then is probably rarely due to the contact of the abscess or suppurating portal vein with the radicles of the bile-duct.

From 115 cases of suppurative pylephlebitis which we have collected from literature, only thirty had icterus. In reviewing the clinical histories of many of these cases it is noticed, however, that icterus followed severe vomiting and disappeared several days after the vomiting ceased, in spite of the fact that the suppurative pylephlebitis went on to a fatal termination.

The location of the abscess also explains the absence of ascites in these cases, the inferior surface of the liver being rarely involved.

The involvement of the peritoneal covering of the liver causes severe pain on respiration, serving to inhibit diaphragmatic breathing, and gives rise to a physical sign which is often of great diagnostic value, viz., a friction that may be palpable as well as audible. The

¹ A. S. Adams: Army Med. Dep. Rep., 1869, xl. 500.

presence of a localized perihepatic friction-sound nearly always is due to one of two things—a gumma or an abscess. A friction-sound when heard between the eighth and tenth ribs in the axillary line is not always distinguishable from one of pleuritic origin. It has, too, been suggested that the friction-sound heard in this area (when caused by an abscess at the dome of the liver) originates from a secondary involvement of the pleural cul-de-sac, and is not due to perihepatitis; be this as it may, a friction-sound heard in this location has enabled the writer to detect the presence of an abscess when no other physical sign of abscess was present than a slight uniform enlargement of the liver. The location of this friction is of value also in determining the point for making an exploratory puncture.

Involvement of the phrenic nerve and the diaphragm is responsible for some of the most constant manifestations of hepatic abscess of amoebic origin.

The phrenic nerve takes its origin from the fourth cervical nerve and often has additional radicles from the third and fifth. Its branches supply the diaphragm, the capsule, and parenchyma of the liver. The right phrenic is the larger and penetrates the left as well as the right lobe of the liver. The phrenic nerve may be responsible for manifestations of irritation of the parenchyma of the liver, irritation or distention of its capsule or of the suspensory ligament, or inflammation of the diaphragm. Phrenic nerve irritation, besides the local pain, often manifests itself in pain in the regions which are supplied by nerves having a common origin with the phrenic. The pain may be referred to the shoulder-joint, scapular, clavicular, or deltoid region, or to the side of the neck, or may even extend down the inner aspect of the arm and forearm. In 163 cases collected by Rouis, he found 28 with pain in the region of the shoulder. Of this number the pain was located in the shoulder-joint 23 times; subscapular and trapezius, 1; external end of clavicle, 1; shoulder and upper arm, 2; shoulder, scapula, and trapezius, 1. The pain lasted in most cases five or six days, and at times five or six months. In one case the referred pain preceded the local pain; in 14 it occurred simultaneously with it; and in 10 cases the shoulder pain commenced after the local pain had commenced.

The pain may be sharp, lancinating, or dull, or simply a sense of tension or fulness in this region. Good proof of ascending neuritis occurring from this source is a case reported by Rouis. A man, aged twenty-three years, had an hepatic abscess which opened externally in the epigastrium. Pain in the deltoid muscle was persistent during the existence of the abscess. After the rupture of the abscess occurred the pain ceased and atrophy of the muscle began. In six months after the abscess had opened the muscle had lost its form entirely.

Tussis hepatica is due (according to Leyden) to phrenic irritation; it may occur with abscess or gallstones, and may also be due to irritation of the liver substance or capsule, or diaphragm or pleura. Rendu had a case in a marine officer returned from Cochín-China, who had persistent cough and fever; tuberculosis of the lungs was suspected. After a few evacuations of stools consisting wholly of pus the cough stopped and did not return.

Hiccough is produced through the agency of the phrenic nerve, and may accompany irritation of the diaphragm or peritoneum; when it occurs in tropical abscess it is said to be evidence of beginning involvement of the diaphragm. Hiccough has been observed in dysentery, where neither diaphragm nor peritoneum was involved.

Diaphragm: the involvement of the diaphragm in tropical abscess has been noticed for many years, but a proper conception of the phenomena that result from it and their diagnostic interpretation is very sparingly treated in even the most recent monographs on liver-abscess. Malcolmson (*Med.-Chir. Trans.*, 1838) calls attention to the fact that the liver is enlarged upward when the abscess is at the dome. In the *Madras Quarterly Medical Journal*, 1844, a writer, in describing an autopsy on a case of tropical abscess, says: "The diaphragm was much attenuated and presented the appearance of a fine, transparent membrane, firmly adherent to the liver posteriorly and superiorly." It has been only within the last few years that clinicians have appreciated the fallacy of the old explanation, viz., that the liver pushes the diaphragm upward. What really happens is this: the diaphragm loses its muscular activity through inflammation and atrophy, so that it no longer resists the elasticity of the lungs. The lungs retract and the diaphragm and liver follow upward, because of the intra-abdominal pressure. In Case II. the lower border of the liver ascended during the week the abscess was growing in size. This was explained at autopsy by the condition of the diaphragm.¹

¹ Since the above was written I have seen, in consultation with Dr. J. Friend, a young man, twenty-one years of age, who gave a history of having had several severe attacks of diarrhoea within the last two years, the last attack, a very severe one, occurring in the summer of 1896. He did not know whether his stools had contained blood or not. He has always lived in Cleveland. After the last attack of diarrhoea his health was relatively good until the latter part of December, when he complained of "a severe cold," with moderate cough and expectoration. For several days before seen by me the patient had repeated chills, followed by a temperature ranging from 99° to 103° and profuse sweating. There was moderate delirium at night. He complained of severe pain over the hepatic area in the axillary and mammary lines. His expectoration became profuse and blood-stained.

I saw the patient on January 2d, when he presented the appearance of a well-nourished and well-developed young man: there was slight cyanosis: the respirations were rapid, costal in character. The pulse was of moderate rate, fair volume, and well sustained. The heart was negative. The lower right thorax and hypochondrium were larger than the corresponding left side. The modified diaphragm-phenomenon—i. e., the band of retraction without the pulmonary excursion—was plainly visible at the fifth rib in the axillary line on the right side, while on the left side the diaphragm-phenomenon, with relatively good pulmonary excursion, was visible at the seventh interspace in the axillary line. There was total absence of reson-

When the diaphragm shares in the process there is another physical sign of considerable value, viz., the dyspnoea, which is rather objective than subjective. The patient may not be cyanotic, but the marked thoracic breathing and diminution of abdominal breathing present the same picture as seen in advanced cases of emphysema. The respiratory excursion of the ribs is very striking, and where there is a question of differential diagnosis between a process in the pleura at the base of the right lung and an abscess at the dome of the liver, the inconsistency between the strong thoracic breathing—*i. e.*, objective dyspnoea—and the extent of thoracic invasion should lead to an exploratory puncture for an hepatic abscess. In a case of bilateral pleurisy with effusion, in which three pints of fluid were withdrawn from each side of the thorax, the objective dyspnoea was not so great as in Case IV. long before rupture into the thorax had taken place.

The observation of the diaphragm-phenomenon as described by Litten¹ is also of value in such cases. In Case IV. the absence or rather diminution of this phenomenon on the right side and its presence on the left side were the points which led to the false diagnosis of neoplasm at the base of the pleura. No more striking example of this misleading sign can be found than the case of Du Pre,² where the incision was made in the fifth intercostal space in the axillary line, several litres of pus evacuated, and the supposed pleural cavity carefully washed out and drained. At the autopsy it was found that an enormous liver-abscess had been opened and that the pleural cavity was free from any inflammatory process.

In the more recent writings on this subject all writers agree upon a certain method of differentiating between the supra- and infraphrenic location of pus. A trocar for exploratory puncture is inserted; if pus flows out during inspiration, it is infraphrenic; if during expiration, it is supraphrenic or intrathoracic.

Dr. Ernst Jendrassik³ describes a case of subphrenic abscess which,

ance and of respiratory sounds on the right side from the fourth interspace in the mammary line and from the fifth rib in the axillary line to the costal border. In the right axillary line from the fifth rib to the costal margin friction-sounds accompanying the respiratory movements were plainly heard. This same area was sensitive to pressure. The right lobe of the liver did not extend below the costal border. The spleen was not palpable, but percussion showed that the anterior border extended one and a half inches above the left costal border. The rest of the abdomen was not sensitive to pressure. There was considerable meteorism. There was abundant purulent expectoration, which was streaked with blood-pigment; was odorless. On microscopical examination no amœbæ, but a few bacteria, were found.

A diagnosis of hepatic abscess with rupture into a bronchus was made, and chloride of ammonium, ten grains six times in the twenty-four hours, was prescribed. In eight days the expectoration ceased, and on January 20th the patient was able to go about. I hear from Dr. Friend that the diaphragm-phenomenon of the right side is now visible at a point symmetrical with that of the left side.

¹ M. Litten: Wiener klin. Wochenschrift, 1895, No. 5.

² Bertrand and Foran.

Jendrassik: Deutsche med. Wochenschrift, 1895.

according to his account, was certainly a tropical abscess at the dome of the liver. The question of diagnosis was between an empyema and subphrenic abscess. The pus flowed out during inspiration. During the operation manometric tracings of the pressure within the abscess-cavity were taken, and showed an increase of pressure with inspiration, which, of course, proved the infraphrenic location of the pus-cavity. This test is sufficient if the pus flows out during inspiration; but if the conditions be the reverse of this, the pus may still be infraphrenic. In Case II., at the time of operation, it was observed that the air rushed into the surgical opening during inspiration and the pus flowed out during expiration, quite the opposite of what we expected after having diagnosed a hepatic abscess with great certainty. The condition at the autopsy sufficiently explained the seeming contradiction. The muscular activity of the right side of the diaphragm was lost. The diaphragm was adherent to the liver posteriorly and superiorly—so firmly, in fact, that the two were removed together. The pleural cul-de-sac was obliterated. During inspiration the ribs were strongly elevated, thus diminishing the tension within the abscess-cavity, and the air rushed in; during expiration the ribs sank down upon the abscess-cavity, thus compressing it and expelling the pus.

The *rôle* this diaphragmatic involvement plays in respiration is seen in comparing Case IV. with the one cited by Bertrand and Foran, that of a young soldier on the march who died suddenly from rupture of a large hepatic abscess into the right thoracic cavity. The area of diaphragm involved must have been very small, else the man could not have performed the duties of a soldier. In Case IV. the respiratory use of the right lung was largely sacrificed before the rupture occurred, so that when it did occur he was very little worse off so far as his respiration was concerned than he was before. The patient had gradually learned to accommodate himself to the loss of respiratory excursion of the right lung.

Urine: the study of the urine in hepatic abscess is very incomplete, and only very limited studies have been made by very few clinicians. In the light of former physiological teaching, great changes in the nitrogen metabolism were expected, and with this idea Dr. Parkes¹ attempted clinically to confirm his preconceived ideas. His deduction was that, owing to the destruction of a large amount of hepatic tissue in tropical abscess, the amount of urea must be diminished in proportion to the extent of hepatic destruction. Since the work of Ponick² and Pody-sowsky, however, we know that as much as two-thirds of the liver of a dog may be removed before there is any disturbance in nitrogen metabolism. Dr. Parkes examined the urine of a man who had an abscess occupying nearly the entire right lobe of the liver. In six days the

¹ Trans. Med. and Phys. Soc., Bombay, 1876, xii. 17.

² Ponick: Virchow's Archiv, 1894

patient received 1152 grains of nitrogen in his food and eliminated 792 grains in the urine, leaving 43 per cent. unaccounted for. The condition of the alimentary tract is not taken into account, simply the nitrogen; none of its combinations was determined.

II. Cook, of Bombay, estimated the urea (Liebig's method) in twenty-one cases of tropical abscess. The amount varied from 42 to 340 grains. These results are very unsatisfactory, as nothing but the urea was determined, and the quantity of nitrogen consumed in the food and eliminated through the intestine was wholly ignored.

Bertrand and Foran claim to have proved the law of Parkes. Their examinations are equally incomplete. One case, however, they report disproves their own argument. In one man the urea had descended to 1.5 grammes in twenty-four hours, at a low body-temperature. Then the temperature rose to 104.5° and the amount of urea eliminated in twenty-four hours rose to 17 grammes, showing that the urea-producing organs were still equal to their task.

In the case of Du Pre, which was operated for empyema and in which at the autopsy there was found scarcely any hepatic tissue left because of the enormous abscess, "the urine was examined by Prof. Bechamp, who, to his great astonishment, could not detect the presence of any urea." Any further chemical analysis is, however, lacking. In Case IV. analyses of the urine were made which show that two-thirds of the liver may be occupied by an abscess and still the nitrogen metabolism be undisturbed. In this case no attempt was made to restrict or determine chemically the diet of the patient, nor was any estimate made of the nitrogen in the stool. The twenty-four hours urine was collected, and the total nitrogen estimated by Kjeldahl's method; the urea by decomposing with hypobromite of sodium, and the resulting nitrogen measured over water, making barometric and thermometric corrections. The ammonia was determined by Schlösing's method as recommended by Neubauer and Vogel; the uric acid by precipitating as ammonium urates with ammonium chloride, dissolving and precipitating as pure uric acid with hydrochloric acid; then titrating it in solution against a known solution of permanganate of potassium. With this method, however, the nitrogen of ammonia is reckoned twice: first, it is decomposed by the hypobromite in estimating urea, and, second, when ammonia as such is determined.

Date.	Amount.	Reaction.	Specific gravity.	Total amount of nitrogen.	Urea.	Nitrogen in urea.	Uric acid.	NH ₃ .
	C.cm.			Grms.	Grms.	Grms.	Grms.	Grms.
July 20th,	840	Acid	1024	13.282	28.0	13.066	0.686	0.8
July 29th,	900	Acid	1020	10.584	20.0	9.32	0.524	1.0
August 5th,	1360	Acid	1013	9.52	15.382	7.158	0.504	0.8

The patient gradually eliminated a smaller amount of urea, but it was because he was eating less and less food—starvation.

TREATMENT. Sachs¹ describes a case of tropical abscess that recovered spontaneously and without rupture. Bertrand and Foran describe a case that was treated surgically and recovered, but later succumbed to another attack of dysentery. At autopsy the scar of the abscess treated surgically was found, but still deeper in the liver-substance and separated from it by normal liver-tissue was a mass the size of a walnut with a thick indurated wall, containing a white creamy substance which proved to consist of calcareous matter and fat, the remains of the abscess that healed spontaneously. Rupture into some neighboring cavity or organ is a very frequent *dénouement* of hepatic abscess. One course, however, merits some consideration, and that is rupture into and expectoration through the right lung. The relative good prognosis in such cases has long been recognized. John Jackson, in the *London Lancet*, 1895, says: "Long experience has convinced me that there is no course which hepatic abscess (when once formed) can take which holds out such good prospects of recovery by natural means as when the channel for the discharge is through the right lung."

Jean L. Morvan (*Thèse de Bordeaux*, 87–88) reports five cases, four of which were expectorated through the right lung and recovered. Brichiteaux (Paris, 1852) reports three cases that recovered after expectorating through the lung. Ughetti collected 131 cases, forty-eight of which were not operated, and 76 per cent. died; forty-five were operated, and 42 per cent. died; thirty-eight broke through the lungs, and 14.6 per cent. died. Sachs reports a case that expectorated only one ounce of pus and recovered. These experiences of other men should make the therapist in cases of suppurative hepatitis very conservative in accepting the value of any medication in the disease.

Dr. Sachs, a German physician in northern Africa, says a Dr. Ori (an Italian physician who had travelled in the Soudan) told him that the natives of that country frequently have hepatic abscesses and operate themselves by opening the abscess with a two-edged knife known as the "chotal." Dr. Ori says they frequently recover when adhesions have been formed between the abdominal parietes and the liver; otherwise they die with peritonitis.

Stewart, an Englishman in the Indian service (*London Lancet*, 1870) says the "Hakeems" of that country treat hepatic abscesses with some success by applying the cautery over the area. Some English writers have applied nitrate of silver over an abscess of the liver to aid the pointing, and, to their surprise, the abscess disappeared entirely. The credit for having made the first free-drainage with stitching the liver

¹ Sachs: *Arch. f. klin. Chirurgie*, 1876, vol. xix.

to the abdominal wall is accorded William Horner, of Philadelphia, in *THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES*, 1834. A diagnosis of hepatic abscess was made and Horner determined to operate. An incision was made at the costal border at the eighth rib, but no adhesions had formed. "In this dilemma I determined to stitch the liver to the side, which was accomplished with a large crooked needle, armed with a ligature of kid-skin and of bulk sufficient to fill up the hole made by the needle. One stitch was made in this way parallel with the upper margin of the incision at the distance of four lines from it and another in the same manner below." Drainage was established by introducing a trocar and allowing it to remain fifty-four hours, then substituted it with a piece of flexible catheter. The patient died on the fourth day. There was no peritonitis.

The surgical treatment is fully discussed in all the monographs on hepatic abscess; the more recent ones, "Langenbuch" and "Bertrand and Foran."

The medical treatment of hepatic abscess has offered very little. Besides the irrigation of the colon with a solution of quinine or of tannic acid during the time of the dysentery, and the administration of calomel and ipecac during the suppurative stage of the hepatitis, there has been little claimed for any therapeutic measure. One therapist, however, has been completely ignored by later writers, and unjustly so if the good results of his treatment are in any degree commensurate with his claims for it.

William Stewart, an army surgeon in the English army in India, published his first article on the subject in the London *Lancet*, 1870. In this article he says that chloride of ammonium had long been in use among the Germans and French for hepatitis when the English used calomel. He describes ammonium chloride therapeutically as a diuretic, diaphoretic, and anodyne. The descriptions of his cases from a diagnostic standpoint are not convincing that it was always hepatic abscess he was dealing with. L. G. Alexander, of Calhoun, Ky., describes a case that he had treated a year before Stewart's publication. The clinical description of the case is fair and rather convincing as to the correctness of the diagnosis (though no exploratory puncture was made). The patient recovered in twenty-three days after commencing the ammonium chloride treatment. One thing, however, is noticeable in the clinical history of the case, and that is, simultaneously with the commencement of the use of ammonium chloride the expectoration increased largely in quantity. The possibility of rupture and expectoration through the right lung was not considered by the author.

In 1879 Stewart published an 8vo. 100-page monograph on the "Treatment of Tropical Abscess with Ammonium Chloride." He describes the remedy as a specific for tropical abscess of the liver. The

patient is put to bed and given as much as 20 grains three or four times a day. In from five to twenty minutes the patient has a feeling of "pins and needles," a sense of warmth, "tearing or pulling," "something gave way," in the right hypochondrium. In some cases the pain or shock would come so suddenly that the patient would cry out. The amount of urine soon increases, the fever diminishes, and the diaphoretic and anodyne action of the drug is apparent. An unfortunate feature about Stewart's cases is that he never proved the presence of pus in a single case by exploratory puncture. Nevertheless, he describes the cases that had enlarged liver, fluctuation, and other clinical signs of liver-abscess that recovered under his treatment.

In one case ammonium chloride was administered where liver-abscess was not suspected; the characteristic symptoms following its use led to the detection of a liver enlarged from the presence of a tropical abscess.

One case of a soldier was treated successfully for liver-abscess. He performed his military duties for two years afterward, when he died from sunstroke. At the autopsy a large puckered scar was found at the dome of the liver where the abscess of two years before was located. Stewart adduces further evidence in the statistics of an English regiment serving seven years in the same and different portions of India. From 1865 to 1869, without the use of ammonium chloride, there were 28 deaths from liver-abscess. From 1869 to 1872 there were 16 diagnoses of liver-abscess and not a single death from the same cause.

In 1889 G. Harrison Younge, of the Indian service, says that ammonium chloride has done valuable service in the military hospitals, as described by Stewart.

In 1891, in the London *Lancet*, Stewart again offers further evidence of the value of ammonium chloride in the treatment of liver-abscess.

In spite of the incomplete clinical account of Stewart's cases, the fact that an English regiment could serve three years in India without a single death from hepatic abscess justifies at least a fair trial of the remedy, which can certainly do no harm.

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